composition containing such oligonucleotide. The invention further relates to a method of use of the DNA and polypeptides for modulating the effect of the B1 protein on the activity of inflammation or cell death or cell survival pathways or any other signaling activity.

The interview among Examiners Davis and Caputa and the undersigned attorney, conducted on August 22, 2002, is hereby gratefully acknowledged. In this interview, all of the outstanding issues were discussed. The examiner stated that the issues would be carefully reconsidered in light of the argument and proposed amendments. The arguments presented at the interview are substantially repeated herein, and the present amendments are as discussed at the interview.

The examiner has repeated and made final the restriction requirement. The examiner states that claims 40-43, drawn to the B1 protein encoded by the claimed polynucleotide will not be examined in this case notwithstanding PCT Administrative Instructions Annex B, Unity of Invention, Part 2, because the protein and DNA are different structures and, thus, could not constitute shared special technical features. The restriction requirement is again respectfully traversed.

The examiner's attention is specifically invited to MPEP §1893.03(d), concerning unity of invention in PCT national stage applications. This passage of the MPEP specifically notes that a corresponding technical feature is exemplified by a key defined by certain claimed structural

characteristics which correspond to the claimed features of a lock to be used with the claimed key. Clearly, everything need not have common structure in order to have shared special technical features. This passage of the MPEP further explicitly notes Examples 1-17 of Annex B, Part II, of the PCT Administrative Instructions. Applicants are relying on Example 17, which is one of those specifically noted with approval by the MPEP. Applicants submit that the examiner is required to follow the MPEP, and accordingly, the protein claims must be examined with the DNA claims. Accordingly, claims 40-43, as well as composition claim 22, which the examiner considers to be patentably indistinct from the protein claims, should be examined in this case.

check Ex. 17

Furthermore, 37 C.F.R. §1.475(b)(3) states that a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to a product, a process specially adapted for the manufacture of the said product, and a use of the said product. The examiner included claims for the method of manufacture in Group I, but did not include a method of use. The examiner should have included the method-of-use of Group IV in Group I. Applicants have elected the method of use claim 49 (previously claim 13) as being the method of use for examination with the product. Dependent claims 14 and 15 should be examined with claim 49. As the examiner has considered that claims 29 and 30 are patentably

check cl 49

indistinct from claim 13 (now claim 49), these should also be examined in the present application.

Claims to all of the remaining groups of invention noted by the examiner have now been deleted without prejudice to the filing of one or more divisional applications thereon. As unity of invention requires that all of the claims of originally indicated Groups I, II and IV be examined in this case, reconsideration and withdrawal of the restriction requirement with respect to all the claims now present in the case is hereby respectfully urged. Applicants reserve the opportunity to file a petition to the Commissioner in this regard in accordance with 37 C.F.R. §1.144.

2nd

Claims 23, 24, 45-47 and 51 have been rejected under 35 U.S.C. §112, first paragraph, as being dependent on non-elected claims. Further, the examiner states that MPEP §821 indicates that, if applicant believes the claims are readable on an elected invention and the examiner disagrees, the claims are vague and indefinite. This rejection is respectfully traversed.

First of all, all of claims 23, 24, 45-47 and 51 have now been amended so as to ultimately depend from claim 44, thus obviating this rejection.

As to the examiner's comments about MPEP §821, it is noted that the examiner is referring to an earlier version of the MPEP. The present version of the MPEP is the 8th Edition, published August 2001. In this edition, MPEP §821 has been revised to delete this sentence. Therefore, the fact that an

examiner and an applicant disagree as to whether the claims are readable on an elected invention is no longer considered to render the claims vague and indefinite within the meaning of 35 U.S.C. §112, second paragraph. Reconsideration and withdrawal of this rejection are, therefore, respectfully urged.

Claims 23, 24, 46 and 47 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite because claim 40, to which these claims depend, recites the language "an amino acid sequence" which encompasses a sequence comprising two amino acids. This rejection is respectfully traversed.

Claim 40 requires that the polypeptide consist of an amino acid sequence encoded by a DNA sequence in accordance with claim 44. No DNA sequence of claim 44 encodes a sequence comprising two amino acids. Reconsideration and withdrawal of this rejection are, therefore, respectfully urged.

Claims 5-8, 11, 44 and 46 have been rejected under 35 U.S.C. §112, first paragraph. The examiner states that the specification does not disclose a DNA sequence encoding an analog of SEQ ID NO:1 having the limitation of "having no more than ten changes" in the amino acid sequence of SEQ ID NO:1. This rejection is respectfully traversed.

The examiner's attention is respectfully invited to page 23, lines 8-11, in conjunction with the disclosure at page 25, lines 6-9, which specifically states that there are preferably no more than ten changes in the amino acid

sequence. Reconsideration and withdrawal of this rejection are, therefore, respectfully urged.

Claims 5-8, 11, 23, 24, 44-48 and 51 have been rejected under 35 U.S.C. §101 because the claims are directed to non-statutory subject matter. The examiner states that the DNA sequence and the encoded polypeptide have the same characteristics and utility as a DNA sequence in a polypeptide found naturally and, therefore, do not constitute patentable subject matter. The examiner suggested amendment of the claims to recite "an isolated DNA sequence" or "an isolated polypeptide".

The claims have now been amended as suggested by the examiner, thus obviating this rejection. It should be understood, however, that applicants intend that the term "isolated" be interpreted as isolated from the natural milieu, and not necessarily isolated from other ingredients of a pharmaceutical composition.

Claims 5-8, 11, 44(c), 47 and 48 have been rejected under 35 U.S.C. §112, first paragraph, as lacking a clear written description of a DNA sequence encoding a fragment of SEQ ID NO:1, which fragment potentiates cell death. The examiner states that, although one could screen for such fragments, the structure of such fragments or their functional characteristics coupled with a known correlation between function and structure or the conserved regions that are critical for the structure and function of the claimed

fragments are not disclosed in the specification. This rejection is respectfully traversed.

First, it is noted that the examiner has withdrawn the part of the rejection relating to analogs of SEQ ID NO:1. Thus, the examiner concedes that the structure of the analogs satisfies the written description requirement, presumably for the reasons set forth in Example 14 of the Examiner Training Materials relating to the written description requirement. However, by the same logic, the fragments should also be acceptable. Just as procedures for making variants that have 95% identity to a sequence and retain its activity are conventional in the art, so are procedures for making fragments of a given sequence that retain their activity. The genus of fragments is not expected to be inordinately large, since all of the fragments must possess the specified activity and must have a sequence that is a part of the sequence of SEQ ID NO:1. The specification teaches how to determine whether any given fragment potentiates cell death. Thus, for the same logic as is provided in Example 14 of the Examiner Training Materials, one of skill in the art would conclude that applicants were in possession of the necessary common attributes possessed by the members of the genus. The structure of the fragments are known because their sequence must appear as part of SEQ ID NO:1. Indeed, for a protein of 540 amino acids, 95% identity allows 27 amino acid residues to vary among 20 different amino acids. The genus of active fragments would be expected to be much smaller than this.

This is another reason why, if the functional analogs of Example 14 are acceptable, the functional fragments must be all the more acceptable. For all of these reasons, reconsideration and withdrawal of this rejection are respectfully urged.

Claims 5-8, 11, 44-47 and 51 have been rejected under 35 U.S.C. §112, first paragraph, for lack of enablement of a DNA sequence "encoding" SEQ ID NO:1. The examiner states that the claims encompass a polynucleotide *in vivo* the amino acid sequence of SEQ ID NO:1. This rejection is respectfully traversed.

The present claims are now directed to isolated sequences. As far this rejection is understood, it is believed that this amendment will obviate the rejection. The term "encoded" is shorthand to cover all codons coding for a polypeptide sequence due to the degeneracy of the genetic code. The claim is not broader than the enabling disclosure. Reconsideration and withdrawal of this rejection is respectfully urged.

Claim 11 has been rejected under 35 U.S.C. §112, first paragraph, as lacking enablement for producing "any polypeptide" that potentiates cell death. The examiner states that the claim does not specify that the polypeptide that potentiates cell death is obtained by expressing a host cell of claim 8. The examiner contends that this claim encompasses polypeptides that potentiate cell death that are other than

those expressed by the cell. This rejection is respectfully traversed.

The term "a polypeptide" in the preamble must be considered in the context of the whole claim. If a host cell of claim 8 makes a polypeptide which potentiates cell death, as would be expected, the method claim is met. The term in the preamble when considered in context does not make the claim broader than the enabling disclosure. Reconsideration and withdrawal of this rejection are, therefore, respectfully urged.

Claims 23, 24 and 51 have been rejected under 35 U.S.C. §112, first paragraph, because the specification does not reasonably provide enablement for a vector encoding a derivative of SEQ ID NO:1.

OK Withdrawn

Claims 23, 24 and 51 have now been amended so as to depend from claim 44, which does not refer to "derivatives". Accordingly, this rejection has now been obviated.

Claim 51 has been rejected under 35 U.S.C. §102(b) as being anticipated by Siyanova. The examiner states that Siyanova teaches a peptide of 66 amino acids in length, which is 100% similar to the claimed SEQ ID NO:1 from amino acid 160 to 168. The examiner states that, given the polypeptide sequence taught by Siyanova, one of ordinary skill in the art would immediately envision the claimed antisense oligonucleotide sequence. This rejection is respectfully traversed.

Claim 51 has now been amended to recite "An oligonucleotide molecule consisting of a sequence encoding an antisense sequence ...". The only part of the sequence of Siyanova that is antisense to SEQ ID NO:1 is a small 9-amino acid stretch of the 66-amino acid peptide. Thus, the 66-amino acid peptide of Siyanova is not a molecule consisting of a sequence encoding an antisense sequence. Thus, it does not anticipate. Reconsideration and withdrawal of this rejection are, therefore, respectfully urged.

Claim 24 has been rejected under 35 U.S.C. §103(a) as being unpatentable over Siyanova in view of Johnstone and Thorpe. The examiner states that Johnstone and Thorpe teach that it was common practice in the art to add a carrier for storage of antibodies and that it would be *prima facie* obvious to add a carrier for storage of the composition of Siyanova. This rejection is respectfully traversed.

Claim 24 has also been amended to specify that the oligonucleotide is a molecule consisting of a sequence encoding an antisense sequence. Thus, even if it were obvious from Johnstone and Thorpe to add a carrier to the 66-amino acid peptide of Siyanova, this would not fall within the scope of claim 24. Furthermore, Johnstone and Thorpe relate to antibodies, while claim 24 relates to an antisense sequence. Antibodies are not oligonucleotide sequences. Thus, there would be no motivation to combine the teachings of Johnstone and Thorpe with Siyanova. Reconsideration and withdrawal of this rejection are respectfully urged.

It is submitted that all the claims now present in the case clearly define over the references of record. Reconsideration and allowance are, therefore, earnestly solicited.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "Version with markings to show changes made".

Respectfully submitted,

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Version with Markings to Show Changes Made

Claims 23, 24, 40, 44-47 and 51 have been amended as follows:

23 (~~Twice~~Thrice-amended). A composition comprising a pharmaceutically acceptable excipient and a recombinant animal virus vector ~~encoding a protein capable of binding a cell surface receptor and encoding said polypeptide according to claim 40~~comprising a DNA sequence according to claim 44.

24 (~~Twice~~Thrice-amended). A composition comprising a pharmaceutically acceptable excipient and an oligonucleotide molecule consisting of a ~~sequence~~ encoding an antisense sequence of at least part of an mRNA sequence ~~encoding a polypeptide~~corresponding to a DNA sequence according to claim ~~40~~44.

40 (~~Amended~~Twice-amended). ~~A~~An isolated polypeptide which potentiates cell death, said polypeptide consisting of an amino acid sequence encoded by a DNA sequence in accordance with claim 44, or a derivative thereof.

44 (~~Amended~~Twice-amended). ~~A~~An isolated DNA sequence encoding a polypeptide which potentiates cell death, said polypeptide consisting of:

(a) a sequence comprising SEQ ID NO:1;

(b) a sequence comprising an analog of (a) having no more than ten changes in the amino acid sequence of (a), each said change being a substitution, deletion or insertion of a single amino acid, which analog potentiates cell death; or

(c) a fragment of the sequence of SEQ ID NO:1, which fragment potentiates cell death.

45 (~~New~~Amended). A DNA sequence ~~encoding a polypeptide~~ in accordance with claim ~~41~~44 encoding a polypeptide of a sequence comprising SEQ ID NO:1.

46 (Amended~~New~~). A DNA sequence ~~encoding a polypeptide~~ in accordance with claim ~~42~~44, encoding a polypeptide consisting of the sequence of (b).

47 (Amended~~New~~). A DNA sequence ~~encoding a polypeptide~~ in accordance with claim ~~43~~44, encoding a polypeptide consisting of the sequence of (c).

51 (~~New~~Amended). An oligonucleotide molecule consisting of a sequence ~~encoding~~ an antisense sequence of at least a part of an mRNA sequence ~~encoding a polypeptide~~corresponding to a DNA sequence according to claim ~~40~~44.

New claims 51 and 52 have been added.

Claims 12, 16, 17, 19, 31-37 and 50 have been deleted.